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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,975	03/30/2005	Sonal Patel	2543-1-036PCT/US	3823

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EXAMINER	
LOCKARD, JON MCCLELLAND	
ART UNIT	PAPER NUMBER
1647	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/509,975	PATEL, SONAL	
	Examiner	Art Unit	
	Jon M. Lockard	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *2-4,6-13,16,18,19 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,14,15,17 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-21* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 October 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/9/05,4/25/05*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Sequence Alignments*.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1, 5, 13-15, 17, and 20, drawn to a method for diagnosing comprising detecting/quantifying SC6 polypeptide in a biological sample, in the reply filed on 11 December 2006 is acknowledged. With regards to the election of species requirement set forth at pg 3-5 of the previous Office Action (08 November 2006), Applicant's election without traverse of cervical cancer as the type of disease/condition in the reply filed on 11 December 2006 is acknowledged. It is noted that the previous Office action (mailed 08 November 2006) incorrectly included claim 13 with groups I and XI, whereas it should have been included in Group XI only (Please see attached Interview Summary). Accordingly, claims 2-4, 6-13, 16, 18, 19, and 21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11 December 2006.

2. The requirement is still deemed proper and is therefore made FINAL.

Status of Application, Amendments, And/Or Claims

3. The Response to the Restriction Requirement filed on 11 December 2006 has been entered in full. Claims 2-4, 6-13, 16, 18, 19, and 21 have been withdrawn from further consideration as discussed above. Therefore, claims 1-21 are pending and claims 1, 5, 14-15, 17, and 20, as they read upon the elected species of cervical cancer, are the subject of this Office

Action. The Examiner recognizes Applicant's right to pursue additional subject matter in other applications.

Information Disclosure Statement

4. The information disclosure statements (IDS) submitted on 09 February 2005 and 25 April 2005 have been considered by the examiner. Reference BB (filed 09 February 2005) has not been considered by the Examiner because a copy of said reference was not received by the Office. 37 CFR 1.98(a)(2) requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed.

Drawings

5. The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference character(s) not mentioned in the description: Figure 4 contains the reference characters BT20, BT474, MCF7, T47D, and MDA 468 which are not mentioned in the Brief Description of the Figures. Corrected drawing sheets in compliance with 37 CFR 1.121(d), or amendment to the specification to add the reference character(s) in the description in compliance with 37 CFR 1.121(b) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any

required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

6. The disclosure is objected to because of the following informalities:

7. The disclosure is objected to because it contains embedded hyperlinks and/or other form of browser-executable code. See for example, pg 6 and 15. Applicant is required to delete the embedded hyperlinks and/or other form of browser-executable code. See MPEP § 608.01.

Appropriate correction is suggested.

8. The disclosure is objected to because of the following informalities: Sequence identifiers are abbreviated throughout the specification as "SEQ ID No." (See pg 3, 4, and 26 for example). The correct format is "SEQ ID NO:#".

Appropriate correction is suggested.

Claim Objections

9. Claim 1 is objected to because of the following informalities: The sequence identifier is abbreviated as "SEQ ID No. 1", the correct format is "SEQ ID NO:1".

Appropriate correction is suggested.

10. Claims 14, 15, 17, and 20 are objected to because of the following informalities: Claims 14, 15, 17, 20, and 21 encompass non-elected inventions, e.g., angiogenesis, angiogenesis related disorders (claims 14 and 17), colon, renal, lung, uterine, breast or pancreatic cell carcinoma, lymphoma, and leukaemia (claims 15 and 20). Appropriate correction is suggested.

Claim Rejections - 35 USC § 112, 2nd Paragraph

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims, 1, 5, 14-15, 17, and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

13. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: comparing the level of SC6 polypeptide in a biological sample obtained from a subject with the level of SC6 polypeptide in a control sample. Therefore, it is unclear what additional method steps are intended to be encompassed by the claim.

14. Claim 1 is further rejected as being indefinite because the claim does not have a step that clearly relates back to the preamble. For example, there is no step indicating the measuring an SC6 polypeptide results in the diagnosis of an individual with a hypoxia related condition, nor is there guidance as to the necessary and significant change or difference in the level of an SC6 polypeptide in an individual with a hypoxia related condition as compared to a normal control. Amending the claim to recite, for example, "wherein an elevated level of said SC6 polypeptide in a test sample relative to the level of said SC6 polypeptide in a normal sample is indicative of a hypoxia related condition", would be remedial with respect to this particular issue.

15. Claim 1 is rejected as being indefinite for reciting the phrase "immunological and/or transporter activity". Without knowing what immunological and/or transporter activity of the

polypeptide with the amino acid sequence of SEQ ID NO:1 the claim is referring to, the metes and bounds of the claim cannot be determined.

16. Claims 1, 14, and 17 are rejected as being indefinite for reciting the term "hypoxia related conditions". The term "hypoxia related conditions" is not defined by the claims, and since neither the art nor the specification provides an unambiguous definition of the term, one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Moreover, it is noted that where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). The term "hypoxia related condition" in claims 14 and 17 is used by the claim to include cancer, angiogenesis, and angiogenesis related disorders, while the accepted meaning is commonly used in the art to refer to a shortage of oxygen in the body as the result of a particular insult or condition, such as ischemic stroke, hemorrhagic stroke, cardiac arrest, carbon monoxide poisoning, for example. Accordingly, the term is indefinite because the specification does not clearly redefine the term.

17. Claims 14 and 17 are rejected as being indefinite for reciting the term "angiogenesis and angiogenesis related disorders". The term "angiogenesis and angiogenesis related disorders" is not defined by the claims, and since neither the art nor the specification provides an unambiguous definition of the term, one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

18. Claims 5, 15, and 20 are rejected for depending from an indefinite claim.

Claim Rejections - 35 USC § 112, 1st Paragraph (Scope of Enablement)

19. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

20. Claims 1, 5, 14-15, 17, and 20 and 11-13 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for a method for diagnosing breast, cervical, colon, renal, lung, or uterine cancer associated with altered expression of an SC6 polypeptide comprising or consisting of the amino acid sequence of SEQ ID NO:1, said method comprising:

a) quantifying in a biological sample obtained from a subject an SC6 polypeptide which comprises or consists of the amino acid sequence of SEQ ID NO:1;

b) comparing the level of said SC6 polypeptide obtained from said subject with level of said SC6 polypeptide in a normal sample, wherein an elevated level of said SC6 polypeptide in a test sample relative to the level of said SC6 polypeptide in a normal sample is indicative of breast, cervical, colon, renal, lung, or uterine cancer,

does not reasonably provide enablement for a method of (1) diagnosing any hypoxia-related condition, (2) diagnosing all cancers (including thymus, pancreatic, lymphoma, and leukaemia), or (3) diagnosing a hypoxia-related condition selected from the group consisting of angiogenesis or angiogenesis-related disorder; nor is it enabling for a method of diagnosing wherein the

method comprises detecting and/or quantifying in a biological sample an SC6 polypeptide which (4) is a variant having one or more amino acid substitutions, deletions, insertions, or modifications relative to the amino acid sequence of SEQ ID NO:1, or (5) is a fragment of a polypeptide consisting or comprising of SEQ ID NO:1 or a variant having one or more amino acid substitutions, deletions, insertions, or modifications relative to the amino acid sequence of SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

21. The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

22. The claims are drawn very broadly to a method for (1) diagnosing any hypoxia-related condition, (2) diagnosing all cancers (including but not limited to cervical, colon, renal, lung, uterine, breast, or pancreatic cell carcinoma, lymphoma, and leukaemia), as well as (3) diagnosing a hypoxia-related condition selected from the group consisting of angiogenesis or angiogenesis-related disorder. While the Specification teaches that the mRNA encoding the SC6 polypeptide of SEQ ID NO:1 is overexpressed in breast, cervical, colon, kidney, lung, and

uterine cancer tissue as compared to matched tissue controls (See Figures 4 and 5), it does not provide adequate guidance for a commensurate number of the claimed species of hypoxia-related disorders, which the specification teaches can be cancer (including but not limited to cervical, colon, renal, lung, uterine, breast, or pancreatic cell carcinoma, lymphoma, leukaemia), angiogenesis and angiogenesis related disorders (which include but are not limited to diabetic retinopathy, asthma, macular degeneration, psoriasis, and rheumatoid arthritis), which are characterized by an overexpression of the SC6 polypeptide.

23. The claims are also drawn very broadly to a method of diagnosing wherein the method comprises detecting and/or quantifying in a biological sample an SC6 polypeptide which (1) is a variant having one or more amino acid substitutions, deletions, insertions, or modifications relative to the amino acid sequence of SEQ ID NO:1, or (2) is a fragment of a polypeptide consisting or comprising of SEQ ID NO:1 or a variant having one or more amino acid substitutions, deletions, insertions, or modifications relative to the amino acid sequence of SEQ ID NO:1. While the specification discloses the mRNA encoding the SC6 polypeptide of SEQ ID NO:1 is overexpressed in breast, cervical, colon, renal, lung, and uterine cancer as compared to matched tissue controls, the specification fails to describe other variants of SEQ ID NO:1, fragments of SEQ ID NO:1 that are at least ten amino acids long, or fragment of a variant of SEQ ID NO:1, wherein the fragment is at least ten amino acids long, which are also overexpressed in breast, cervical, colon, renal, lung, and uterine cancer; nor does the specification provide adequate guidance on how to make variants of SEQ ID NO:1 that exhibit the same immunological and/or transporter activity of SEQ ID NO:1, and it is not at all predictable that they would be diagnostic of a hypoxia-related condition, and it would require

undue experimentation to determine such. Other than the polypeptide of SEQ ID NO:1, the disclosure fails to provide sufficient guidance and information regarding the structural and functional requirements commensurate in scope with what is encompassed by the instant claims. The disclosure has not shown (1) which portions of the polypeptide SEQ ID NO:1 are critical to the activity of the polypeptide of SEQ ID NO:1; (2) what modifications e.g., substitutions, deletions, or insertions) one can make to SEQ ID NO:1 that will result in polypeptide variants with the same function/activity as the polypeptide of SEQ ID NO:1; and (3) any guidance on how to use the polypeptides variants of SEQ ID NO:1 which are not disclosed as being differentially expressed in a hypoxia-related condition. The state of the art is such that the relationship between the sequence of a protein and its activity is not well understood and unpredictable, and that certain positions in the sequence are critical to the protein's structure/function relationship and can only tolerate only relatively conservative substitutions or no substitutions.

24. The problem of predicting protein and DNA structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and DNA is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-

8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the encoded protein which are tolerant to change (e.g. such as by amino acid substitutions, deletions, or insertions), and the nature and extent of changes that can be made in these positions and still retain the activity of the polypeptide of SEQ ID NO:1. As the specification does not teach how to make and use a number of species that would be commensurate in scope with the claims, it would require undue experimentation for one skilled in the art to practice the invention in a manner commensurate in scope with the claims, given the lack of guidance in the specification and the very broad scope of the claims.

25. Due to the large quantity of experimentation necessary to screen the infinite number of "hypoxia-related conditions" that are characterized by an overexpression of the SC6 polypeptide of SEQ ID NO:1; to generate the infinite number of derivatives recited in the claims and screen the same for activity and differential expression; the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity; the complex nature of the invention; and the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 112, 1st Paragraph (Written Description)

26. Claims 6-9 and 11-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

27. The claims are drawn very broadly to a method of diagnosing wherein the method comprises detecting and/or quantifying in a biological sample an SC6 polypeptide which (1) is a variant having one or more amino acid substitutions, deletions, insertions, or modifications relative to the amino acid sequence of SEQ ID NO:1, or (2) is a fragment of a polypeptide consisting or comprising of SEQ ID NO:1 or a variant having one or more amino acid substitutions, deletions, insertions, or modifications relative to the amino acid sequence of SEQ ID NO:1. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, and any combination thereof. In this case, the only factor present in the claims is a recitation of a partial structure and a desired functional property in the form of the recitation of exhibiting the immunological and/or transporter activity of the polypeptide with the amino acid sequence of SEQ ID NO:1. However, there does not appear to be an adequate written description in the specification as filed of any essential structural feature common to

molecules that exhibit the immunological and/or transporter activity of the polypeptide with the amino acid sequence of SEQ ID NO:1 or are differentially expressed in breast, cervical, colon, renal, lung, and uterine cancer. While the specification provides adequate written description for an SC6 polypeptide consisting of SEQ ID NO:1 and an SC6 polypeptide comprising the amino acid sequence of SEQ ID NO:1, it does not provide adequate written description for a commensurate number of the claimed species of agents that exhibit the immunological and/or transporter activity of the polypeptide with the amino acid sequence of SEQ ID NO:1 or are differentially expressed in breast, cervical, colon, renal, lung, and uterine cancer. The distinguishing characteristics of the claimed genus are not described. The only adequately described species are an SC6 polypeptide consisting of SEQ ID NO:1 and an SC6 polypeptide comprising the amino acid sequence of SEQ ID NO:1. Accordingly, the specification does not provide adequate written description of the claimed genus.

28. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

29. With the exception of the Sc6 polypeptides referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed SC6 polypeptides, variants, and fragments thereof, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate

written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The product itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

30. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

31. Therefore, only an SC6 polypeptide consisting of SEQ ID NO:1 and an SC6 polypeptide comprising the amino acid sequence of SEQ ID NO:1, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

32. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the

international application designated the United States and was published under Article 21(2) of such treaty in the English language.

33. Claims 1, 5, 14, and 17 are rejected under 35 U.S.C. 102(e) as being anticipated by Sanjanwala et al. (WO 01/090148 A2, filed 17 May 2001).

34. Sanjanwala et al. teach a human neurotransmitter transporter designated NTT-4 (SEQ ID NO:4). NTT-4 comprises an amino acid sequence that shares 98.6% sequence identity to SEQ ID NO:1 of the instant application (See attached Sequence Alignment). Sanjanwala et al. also teach that antibodies which bind to the NTT-4 protein may be used for the diagnosis of disorders characterized by expression of NTT-4 (See pg 58, lines 10-13), including but not limited to hypoxia-related condition such as diabetic neuropathy, ischemic cerebrovascular disease, and stroke, as well as prostate cancer (See pg 59-60). Thus, Sanjanwala et al. meets all the limitations of claims 1, 5, 14, and 17.

Summary

35. No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon M. Lockard, Ph.D. whose telephone number is (571) 272-2717. The examiner can normally be reached on Monday through Friday, 7:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached on (571) 272-0961.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon M. Lockard, Ph.D.
March 3, 2007

CHRISTINE J. SAOUD
PRIMARY EXAMINER

Christine J. Saoud

Sequence Alignment

```
<!--StartFragment-->
RESULT 7
AAE14406
ID   AAE14406 standard; protein; 649 AA.
XX
AC   AAE14406;
XX
DT   26-MAR-2002  (first entry)
XX
DE   Human neurotransmitter transporter, NTT-4.
XX
KW   Human; neurotransmitter transporter; NTT-4; transport disorder;
KW   neurological disorder; psychiatric disorder; diabetes mellitus;
KW   amyotrophic lateral sclerosis; Parkinson's disease; prostate cancer;
KW   cardiac disorder; angina; Alzheimer's disease; amnesia; epilepsy;
KW   sickle cell anaemia; stroke; Huntington's disease; psychiatric disorder;
KW   acute stress disorder; anorexia nervosa; transgenic animal; gene therapy;
KW   sodium:neurotransmitter symporter family; SNF.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Domain          109. .128
FT                   /label= Transmembrane_domain
FT   Domain          418. .436
FT                   /label= Transmembrane_domain
FT   Domain          495. .513
FT                   /label= Transmembrane_domain
FT   Domain          536. .553
FT                   /label= Transmembrane_domain
XX
PN   WO200190148-A2.
XX
PD   29-NOV-2001.
XX
PF   17-MAY-2001; 2001WO-US016283.
XX
PR   19-MAY-2000; 2000US-0205518P.
PR   22-JUN-2000; 2000US-0213956P.
PR   28-JUN-2000; 2000US-0215105P.
PR   14-JUL-2000; 2000US-0218947P.
PR   27-JUL-2000; 2000US-0221488P.
XX
PA   (INCY-) INCYTE GENOMICS INC.
XX
PI   Sanjanwala MS,  Walia NK,  Tribouley CM,  Yue H,  Gandhi AR,  Ding L;
PI   Yao MG,  Lal P,  Baughn MR,  Hafalia A,  Elliott VS,  Patterson C;
PI   Rankumar J;
XX
DR   WPI; 2002-097640/13.
DR   N-PSDB; AAD23976.
XX
PT   Novel human neurotransmitter transporter polypeptides and polynucleotides
PT   for diagnosing, preventing or treating transport, neurological and
PT   psychiatric disorders and for identifying modulators of therapeutic use.
XX
PS   Claim 1; Page 114-116; 123pp; English.
XX
CC   The present sequence is human neurotransmitter transporter (NTT)-4
CC   (Incyte ID No: 71556695CD1). The NTT-4 polypeptide contains
CC   sodium:neurotransmitter symporter family (SNF) signature sequences. The
CC   NTT polypeptide and polynucleotide are useful for diagnosis, treatment
CC   and prevention of transport, neurological and psychiatric disorders.
CC   Transport disorders include akinesia, amyotrophic lateral sclerosis,
CC   ataxia telangiectasia, cystic fibrosis, Becker's muscular dystrophy,
CC   diabetes mellitus, diabetes insipidus, myasthenia gravis, myocarditis,
CC   Parkinson's disease, prostate cancer; cardiac disorders associated with
CC   transport include angina, bradyarrhythmia, dermatomyositis, polymyositis;
CC   neurological disorders associated with transport include Alzheimer's
CC   disease, amnesia, bipolar disorder, dementia, depression, epilepsy,
CC   Tourette's disorder, schizophrenia, and other disorders associated with
CC   transport include neurofibromatosis, sickle cell anaemia, Wilson's
CC   disease, cataracts, infertility, hyperglycaemia, hypoglycaemia, Graves'
CC   disease, goitre, Cushing's disease, hypercholesterolaemia and cystinuria.
CC   Neurological disorders treatable include epilepsy, stroke, Huntington's
CC   disease, dementia, and other extrapyramidal disorder, motor neuron
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CC   disorders, prion disease including kuru, metabolic disease of the nervous
CC   system, and other developmental disorders of the central nervous system,
CC   neuromuscular disorders, metabolic, endocrine and toxic myopathies,
CC   periodic paralysis, mental disorders including mood and anxiety.
CC   Psychiatric disorders include acute stress disorder, alcohol dependence,
CC   anorexia nervosa, anxiety, obsessive-compulsive disorder, panic disorder
CC   and sleep disorder. The polynucleotide is useful for creating knockin
CC   humanised animals or transgenic animals to model human disease and to
CC   detect and quantify gene expression in biopsied tissues in which
CC   expression of NTT is correlated with disease. The polynucleotide is also
CC   useful for generating hybridisation probes useful in mapping the
CC   naturally occurring genomic sequence and oligonucleotide primers derived
CC   from it are useful to detect single nucleotide polymorphisms. NTT, its
CC   fragments and antibodies are useful as elements on a microarray which is
CC   useful to monitor or measure protein-protein interactions, drug-target
CC   interactions and gene expression profiles. Sequences of the NTT
CC   polypeptide are used to analyse the proteome of a tissue or cell type.
CC   The polypeptide of the invention is also useful for screening its
CC   agonist, antagonist, modulator or a compound that binds to it
XX
SQ   Sequence 649 AA;

  Query Match             98.6%;  Score 3291.5;  DB 5;  Length 649;
  Best Local Similarity   98.9%;  Pred. No. 0;
  Matches  613;  Conservative    2;  Mismatches    4;  Indels    1;  Gaps    1;

Qy          1 MATKEKLQCLKDFHKDMVKPSPGKSPGTRPEDEAEGKPPQREKWSSKIDFVLSVAGGFVG 60
              ||||||||||||||||::||||||||||||||||||||||||||||||||||||||||||
Db         30 MATKEKLQCLKDFHKDILKPSPGKSPGTRPEDEAEGKPPQREKWSSKIDFVLSVAGGFVG 89

Qy         61 LGNVWRFPYLCYKNGGGAFLIPYFIFLFGSGLPVFFLEIIIGQYTSEGGITCWEKICPLF 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         90 LGNVWRFPYLCYKNGGGAFLIPYFIFLFGSGLPVFFLEIIIGQYTSEGGITCWEKICPLF 149

Qy        121 SGIGYASVVIVSLLNVYYIVILAWATYYLFQSFQKELPWAHCNHSWNTPHCMEDTMRKNK 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        150 SGIGYASVVIVSLLNVYYIVILAWATYYLFQSFQKELPWAHCNHSWNTPHCMEDTMRKNK 209

Qy        181 SVWITISSTNFTSPVIEFWERNVLSLSPGIDHPGSLKWDLALCLLLVWLVCFFCICKGVR 240
              |||||||||||||||||||||||||||||||||||||||||||||||||||| ||||
Db        210 SVWITISSTNFTSPVIEFWERNVLSLSPGIDHPGSLKWDLALCLLLVWLVCFFCIWKGVR 269

Qy        241 STGKVVYFTATFPFAMLLVLLVRGLTLPGAGRGIKFYLYPDITRLEDPQVWIDAGTQIFF 300
              |||||||||||||||||||||||||||||| ||||||||||||||||||||||||||||
Db        270 STGKVVYFTATFPFAMLLVLLVRGLTLPGAGAGIKFYLYPDITRLEDPQVWIDAGTQIFF 329

Qy        301 SYAICLGAMTSLGSYNKYKYNSYRDCMLLGCLNSGTSFVSGFAIFSILGFMAQEQGVDIA 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        330 SYAICLGAMTSLGSYNKYKYNSYRDCMLLGCLNSGTSFVSGFAIFSILGFMAQEQGVDIA 389

Qy        361 DVAESGPGLAFIAYPKAVTMMPLPTFWSILFFIMLLLLGLDSQFVEVEGQITSLVDLYPS 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        390 DVAESGPGLAFIAYPKAVTMMPLPTFWSILFFIMLLLLGLDSQFVEVEGQITSLVDLYPS 449

Qy        421 FLRKGYRREIFIAFVCSISYLLGLTMVTEGGMYVFQLFDYYAASGVCLLWVAFFECFVIA 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        450 FLRKGYRREIFIAFVCSISYLLGLTMVTEGGMYVFQLFDYYAASGVCLLWVAFFECFVIA 509

Qy        481 WIYGGDNLYDGIEDMIGYRPGPWMKYSW-VITPVLCVGCFIFSLVKYVPLTYNKTYVSPT 539
              |||||||||||||||||||||||||||| |||||||||||||||||||||||||||| |
Db        510 WIYGGDNLYDGIEDMIGYRPGPWMKYSWAVITPVLCVGCFIFSLVKYVPLTYNKTYVYPN 569

Qy        540 WAIGLGWSLALSSMLCVPLVIVIRLCQTEGPFLVRVKYLLTPREPNRWAVEREGATPYNS 599
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        570 WAIGLGWSLALSSMLCVPLVIVIRLCQTEGPFLVRVKYLLTPREPNRWAVEREGATPYNS 629

Qy        600 RTVMNGALVKPTHIIVETMM 619
              ||||||||||||||||||||
Db        630 RTVMNGALVKPTHIIVETMM 649

<!--EndFragment-->
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